

Serial No: 09/540,963

- 2 -

Art Unit 1632

providing isolated dendritic cells which are genetically modified to express on the cell surface a selectin polypeptide comprising an endothelial selectin ligand binding portion of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin, and administering the isolated genetically modified dendritic cells to the subject.

28.(amended) A composition comprising isolated dendritic cells which are genetically modified to express on the cell surface a selectin polypeptide comprising an endothelial selectin ligand binding portion of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin.

Remarks

Claims 1, 5 and 28 were amended to clarify the nature of the genetic modification of the dendritic cells in the claimed methods and compositions. As amended, the claims recite that the dendritic cells are genetically modified to express on the cell surface a selectin polypeptide. The passages in the application that literally support these amendments are as follows: the first sentence of the Abstract; page 3, lines 6-7; and page 7, lines 1-2. No new matter has been added.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1, 5-7, 12-14, 18-21, 25, 28-30, 36-37 and 48 under 35 U.S.C. § 112, first paragraph as not enabled by the specification. Applicants respectfully traverse the rejection.

The claimed invention is based in part on Applicants' recognition that dendritic cells expanded *in vitro* have a reduced expression of L-selectin as compared to dendritic cells freshly isolated from a subject. This reduced expression was demonstrated to result in the inability of the dendritic cells to bind selectin ligands. Sufficient expression of selectins is needed to allow the dendritic cells to enter the lymph nodes and result in the activation of naïve T cells, an action which is mediated efficiently by dendritic cells. Applicants demonstrated that it is likely that L-selectin is cleaved or digested because expression of exogenously added L-selectin by retroviral transduction does not result in increased expression of L-selectin. Further, transduction with an E/L-selectin chimera which is not cleaved or digested results in targeting to secondary lymphoid tissues. It is important to note that the known binding between selectins and selectin ligands expressed on cell surfaces means that dendritic cells that express selectins can be targeted to